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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/978,593
Filing Date: October 18, 2001
Appellant(s): AYISI, NANA K.

Elizabeth A. Hayes-Quebec
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed August 26, 2005 appealing from the Office action mailed April 19, 2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows:

Whether claims 20, 22, 31 and 32 satisfy the 35 U.S.C. § 112 first paragraphs. Appellants brief appeared to have a typographical error, claim 20 was not accounted for.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Planchon et al., Differential effect of butyrate derivatives on human breast cancer cells grown as organotypic nodules in vitro and as xenografts in vivo, In Vivo (1992) Vol. 6, pages 605-610.

Kerr et al., The relationship between cytotoxic drug exposure and tumor cell kill *in vitro* and in *vivo*, In Vivo (1991) Vol 5, pages 385-388.

Chomienne et al., Discrepancy between *in vitro* and *in vivo* passaged U-937 human leukemic Cells: Tumerorigenicity and sensitivity to differentiating drugs. In Vivo (1988) Vol. 2, pages 281-288.

Washington Times Article by Joyce Howard Price, November 16, 2001, page 3.

Kirsi et al., Broad Spectrum antiviral cavity of 2-beta-d ribofuranosylselenzaole-carboxaimde, a new antiviral agent, Antimicrobial Agents and Chemotherapy (1983) Vol. 24, No. 3, pages 353-361

Mitsuya et al., Suramin protection of T Cells *in vitro* against infectivity and cytopathic effect of HTLV-III. Science, (1984) Vol. 226, pages.172-174.

Sanstrom et al., Antiviral Therapy in AIDS: Clinical and pharmacological properties and therapeutic experience to date. Drugs (1987) Vol. 34, pages 372-390.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 20, 22, 31 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting HIV viral replication in Vero cells and in Molt4 clone 8 cells with an extract of *O. gratissimum*, does not reasonably provide enablement for the *O. gratissimum* extract to inhibit HIV viral replication in a mammal or in any other cell line. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Characteristics of a compound's activity *in vitro* using purified or partially purified components generally differs significantly with the compound when used in a living body.

There is insufficient guidance and objective evidence that such teachings would be indicative of the effect of *O. gratissimum in vivo*, i.e. in an individual; wherein it would not be predictable to one of skill in the art to use the method in order to treat HIV viral infection in any individual. Those of skill in the art recognize that *in vitro* assays and/or cell-cultured based assays are generally useful to observe basic physiological and cellular phenomenon when screening the effects of potential drugs. However, clinical correlation is generally lacking. Cultured cell lines generally differ significantly from *in vivo* animal models. In an animal the compound must be delivered into the circulation in a sufficient concentration and for a sufficient period of time. *In vitro* assays cannot duplicate the complex conditions of *in vivo* therapy. In addition, variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful therapy with the compound. The composition may be inactivated *in vivo* before producing a sufficient effect, for example, by proteolytic degradation or immunological activation. The composition may not otherwise reach the target because of its inability to penetrate tissues or cells where its activity is to be exerted. Fluids, cells and tissues may absorb the composition so that it has not effect. The circulation in the target area may be insufficient to carry the composition to the area in high enough concentration.

The greatly increased complexity of the *in vivo* environment as compared to the very narrowly defined and controlled conditions of an *in vitro* assay does not permit a single extrapolation of *in vitro* assays to human diagnostic efficacy with any reasonable degree of predictability. *In vitro* assays cannot easily assess cell-cell interactions that may be important in a particular pathological state. Furthermore it is well known in the art that cultured cells, over a period time, lose phenotypic characteristics associated with their normal counterpart cell type.

The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation *in vivo*. Without this control, cellular metabolism may be more constant *in vitro* but may not be truly representative of the tissue from which the cells were derived. For example in an *in vitro* tumor cell assay the cells exhibited growth inhibition when treated with a compound in the test tube. When the same compound was used in an animal there was no growth inhibition of the tumor cell (see Planchon et al., In Vivo, 1992, see abstract; Kerr et al., In Vivo, 1991, pages 385-388). This is not an isolated observation, in another *in vivo* vs. *in vitro* model, passaged U-937 human leukemic cells behaved differently when these cells are passage *in vitro* or *in vivo* (see Chomienne et al., In Vivo, 1988, pages 281-288). Passageing the U-937 cells in mice resulted in the cells losing the ability to differentiate when exposed to differentiating drugs (see Figure 6). There was no explanation for this dedifferentiation phenomenon for leukemic cells, but it is clear that host factors play an important role, either in selecting pre-existing less differentiated cells or by inducing modifications in the cells' proliferation/differentiation status (see Chomienne et al., page 286, column 1, 1st paragraph). Clearly it is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and thus a cell in culture cannot duplicate the complex conditions of the *in vivo* environment involved in host-tumor and cell-cell interactions.

In a statement by Joanne Schellenbach, spokeswoman for the American Cancer Society, regarding the "smart bomb" for the use of cancer treatment after a study in animals (see Washington Times Article by Joyce Howard Price, November 16, 2001, p. 3) she noted that "results of animal studies cannot always be easily replicated in humans." In fact, she said, "not a large percentage" of promising results in animal studies "pan out" for use in humans. Thus,

more than just *in vitro* studies will be needed in order to show efficacy for using a particular drug in a human being in hopes to treat a condition.

The effect of an inhibitor is also dependent on the virus, inhibitor concentration and cell line used (see Kirsi et al., 1983, pages 353-361). The experiments in the study were controlled for the (i) number of times the cells were passaged (ii) the drug lot and dilution used (iii) the conditions under which the virus pool was frozen (iv) the amount of virus added to each well. The study looked at several different DNA and RNA viruses and tested them against three different inhibitor compounds (see Kirsi et al., see table 2). The results indicate (see Kirsi et al., see table 2) that the inhibitor may be effective in one cell line but not in another cell line for the same virus.

Furthermore, inhibiting the replication/infection of a virus *in vitro* with a compound would not provide evidence that the compound would inhibit the intact virus from infecting its target cell *in vivo*. The example of suramin, this drug was shown to be very promising in *in vitro* studies to block the infectability of HIV (see Mitsuya et al., 1984, pages172-174). Further studies using suramin as an anti-AIDS drug contradicted the results expected from the *in vitro* tests. These studies (see Sandström et al., 1987, pages 372-390) showed that in *in vivo* experiments using suramin demonstrate no significant clinical or immunological improvement and the net effect of suramin was in fact harmful. Therefore, the use of *in vitro* tests is not an acceptable predicator of *in vivo* activity when claiming treatments to HIV.

Claims 20 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by El-Said et al. (Planta Medicine, 1969). The rejection is evidenced by the Merck Manual (Ed. Beers et al., Published by Merck Research Laboratories, Whitehouse Station, N.J. (1999) pp 1293-1296, 1303-1306, 1312-1323, 2320-2324 and 2341-2343).

The instant invention reads on a treatment of a viral infection *in vivo* using an extract of *Ocimum gratissimum*. The aqueous extract of the instant invention is prepared by boiling the leaves, seeds, fruits, stems, barks or roots of the plant for 10 minutes in distilled water. El-Said et al. disclose that an aqueous extract of *O. gratissimum* has been used in Nigerian herbal medicine for the treatment of fevers (see abstract). Fever is a symptom that is associated with viral or bacterial infections (as evidenced by the Merck Manual). Thus, the treatment of viral infection using an extract of *O. gratissimum* is anticipated by El-Said et al.

A claim is anticipated if each and every element is expressly or inherently described in the art reference (MPEP 2131) and a reference contains an enabling disclosure if the public was in possession of the claimed invention before the date of the invention (MPEP 2121.01). In this instant the prior art discloses the decoction (boiling leaves in water like tea) of *O. gratissimum* for the treatment of fever and diaphoretic and also as a stomachic laxative. Where a method of the prior art is performed on either the same population or a subset of the same population as the claimed method using the same material and methodology, the prior art method inherently would achieve whatever desired outcome was discovered and claimed by applicant. In this instance Nigerian people used an infusion of the *O. gratissimum* for the purpose of treating fevers. Fevers are a response by the body to combat bacterial or viral infections. The Nigerian patient may not have appreciated the nuance that a compound found in the plant actually has a cytopathic effect

on a virus in a test tube. The purpose of drinking the infusion of *O. gratissimum* by the Nigerian patient is to help the patient get well. The prior art discloses a method of administering an extract of *O. gratissimum* to a patient and the compounds responsible for inhibiting a virus would inherently be present in the extract. *In re Cruciferous Sprout Litigation*, 64 USPQ2d 1202 (CA FC 2002).

The claims broadly interpreted can include the treatment of cells as they are found in an individual. The mere recitation of newly discovered function or property, inherently possessed by things in the prior art, does not cause the claim drawn to those things to distinguish over the prior art (See *In re Best, Bolton, and Shaw* 195 USPQ 430 (CCPA 1977), *In re Schreiber* 44 USPQ2d 1429).

Because El-Said et al. discloses the use of an extract of *O. gratissimum* for the treatment of fevers (see abstract) the instant claims are anticipated. *O. gratissimum* has been used in Nigerian herbal medicine to treat fevers, and fever is a symptom that is associated with viral or bacterial infections. Thus, the claims are anticipated by El-Said et al.

(10) Response to Argument

Issue 1 - 35 USC §112 first paragraph.

(1) Therapeutic effect of *Ocimum gratissimum*. Applicants cite *In re Borokowski* (422 F2d 904, 164 USPQ 642 (CCPA1970)) for the proposition that the examiners analysis in the claim rejection was improper. Applicant argues that it is inappropriate to "study appellants disclosure, to formulate a conclusion as to what he (the examiner) regards as the broadest

invention supported by the disclosure, and then to determine whether appellants claims are broader that the examiners conception of what the invention is."

In response, Office personnel are to give claims their broadest reasonable interpretation in light of the supporting disclosure. *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997). In this instance interpreting the claims as including treatment in a patient does not require a study of the disclosure.

Applicants cite *In re Bundy* (209 USPQ 48 (CCPA 1981) for the proposition that "the *in vitro* data provides sufficient information as an initial starting point so that one of skill in the art could determine, without inventive skill or undue experimentation, the necessary strength or concentration of the plant extract to achieve the desired pharmacological effect *in vivo, i.e.,* the inhibition of HIV replication in mammalian or human cells."

In response, the facts of *in re Bundy* can be distinguished from the facts of the instantly claimed invention. In B*undy* the question was whether prostaglandin analogs had the same effect as prostaglandin. At the time of filing, the claims in *Bundy,* prostaglandin was a known compound with known *in vivo* activity. Prostaglandin was tested in patients and the activity was known. In the instant case the composition was only tested in the test tube. There was no evidence in *Bundy* that the prostaglandin analogs, which are based on the same core structure of prostaglandin, would not act similarly. In the instant invention Appellants are claiming a composition that is a plant extract with a particular effect on virally infected cells in the test tube. The instant invention was rejected on the grounds of not being enabled by not providing enough information on "how-to-use" the particular composition for the treatment of a viral infection in a

patient (the broadest interpretation of the claim). The instant specification has only provided *in vitro* data for the plant extract, thus, the mechanism of how the composition functions in a patient is not known. This is different from the facts in *Bundy* where the effect of the core structure of prostaglandin was known in the prior art. In the instant invention we do not know the core structure of the active compound and the function of the core structure in the patient. The art is replete with showings that *in vitro* findings cannot be extrapolated to *in vivo* therapies. This differs from the prostaglandin analogs of *Bundy* in which the prostaglandin core structure was shown to have an effect *in vivo*. The selectivity of the prostaglandin analog activity *in vitro* was with respect to potency and not biological activity. Thus *Bundy* differs from the instant invention in that the structure and use of prostaglandin was known at the time the analogs were claimed. In this case appellants are claiming a method of treatment based on the effect of the composition on a virus in the test tube. The Office has maintained that the *in vitro* examples provided by appellants' disclosure are insufficient for claiming the treatment of HIV in a patient. There is no showing that sufficient amount of the composition can be giving to the HIV infected patient to effectuate a treatment without being lethal to the patient.

(2) Correlation of *in vitro* testing to *in vivo* efficacy. Appellants argument regarding the Sandström et al. reference are (a) "the reference is limited to two specific anti-viral compounds that are unrelated to an extract of *O. gratissimum*" (arguing that there is no relation of the prior art compound to the compound of the instant invention); and (b) "that the reference is not relevant to the state of the rapidly developing HIV art as of the filing date of the instant application 10 years later (i.e. in Dec 1997)" (arguing age of reference).

In response (a), the Sandstrom et al. reference was cited for the observation made using the drug suramin. The reference was not cited for the purpose of showing any kind of structural relatedness of AZT or suramin to the extract of *O. gratissimum*. Suramin was shown in the prior art to be very promising to block the infectability of HIV (see Mitsuya et al., Science, (1984) Vol. 226, pp.172-174). However, after further studies using suramin as an anti-AIDS drug in a patient, the results from the patient contradicted the expected results from the *in vitro* tests. Studies (see Sandström et al. Drugs (1987) pages 372-390) showed that *in vivo* experiments using suramin demonstrated no significant clinical or immunological improvement and the net effect of suramin was in fact harmful to the patient. Thus the Sandström et al. reference was used to bolster the arguemnt that *in vitro* effects cannot be extrapolated to *in vivo* HIV therapies.

In response (b) to Appellant's argument based upon the age of the references is not persuasive. Contentions that the references are old are not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977). Appellant's argument that the Sandström et al. reference is not relevant art in the rapidly developing HIV field is not persuasive. Although, there have been many new discoveries in the past 20 years regarding HIV, the observations made by references early in the art are still relevant for what the references teach. In this instance the reference was cited for the teaching that suramin effects *in vitro* could not be used to extrapolate the effect of suramin in a patient. Here suramin could not be given to a patient at sufficiently high concentration to effect HIV replication in the patient without having a toxic side effect on the patient. The argument that the art has develop

significantly from that time period is not relevant to the observation that *in vitro* assays cannot predict *in vivo* results.

(3) Working examples and guidance in the specification. Applicants argue that MPEP § 2164.02 does not require a rigorous or invariable exact correlation between the *in vitro* and *in vivo* model. Applicants cite *In re Brana*, 51 F3d 1560, 34 USPQ2d 1436, (Fed. Cir. 1995) for the specific emphasis that in the *Brana* decision the Court revered the PTO finding that *in vitro* data did not support *in vivo* applications. "If the art is such that a particular model is recognized as correlating to a specific condition then it should be accepted as correlating unless the examiner has evidence that the model does not correlate."

In response, the Office has cited evidence that the tissue culture based assay model does not correlate to the effect of the drug in the patient. The Office has shown that there is no correlation between an *in vitro* model and an *in vivo* effect for the treatment of HIV in a person because the medicament may not be able to be given at high quantities to be an effective treatment and it may not even be effective at doses that are toxic to a person. If a compound is toxic at concentrations that inhibit HIV replication in the patient it cannot be considered a therapy.

Appellants cite *Cross v. Iizuka*, 224 USPQ 739 (Fed Cir. 1985) for the proposition that "a rigorous or an invariable exact correlation is not required."

In response, *in vitro* testing permits an investigator to establish the potency of a compound with respect to the particular pharmacological activity. In this case, regarding HIV, it

is well established in the art that what is observed in the test tube does not necessarily pan out as treatment method in the patient. This lack of correlation was exemplified in the case of suramin where the drug was effective in a test tube but could not be given to a patient in high enough concentration to be an effective treatment (see Sandström et al.). Thus the Sandström et al. reference was used to establish that *in vitro* effects couldn't be extrapolated to *in vivo* HIV therapies.

Even when using well-known cell lines, the information obtained from the cell lines does not necessarily provide any information regarding the effect of the product *in vivo*. In the HIV art there are numerous examples in which laboratory strains of the virus are used for testing purposes in the lab and the products are found to be effective in the *in vitro* setting against a laboratory strain of HIV. However, the effectiveness of the treatment tested *in vitro* has not panned out in the clinical setting where the virus in a patient is a wild type virus and not the laboratory strain. The best example comes form the repeated efforts of trying to develop a vaccine for the purpose of antibody production in the patient that would be effective at preventing viral entry in the cells *in vivo*. These antibodies, although effective against the laboratory strains, have not proven effective *in vivo* against wild type virus in the environment. The Office recognizes that FDA approval is not a prerequisite for finding utility (25 U.S.C. § 101) for purposes of patentability as pointed in *In re Brana*, 34 USPQ 2d 1436 (Fed. Cir. 1995). In this instance utility was not questioned, the instant claims are rejected for failure to teach "how to use" the claimed invention in the unpredictable art of viral treatments.

Appellant argues that the claims are directed only to subject matter, which appellant alleges is enabled in the specification. The specification is enabled for the treatment of HIV

infected cells when they are in found in a tissue culture plate (petri dish) *in vitro*. The claims are not limited to the treatment of HIV infected cells *in vitro*, the claims broadly interpreted can include the treatment of cells as they are found in an individual and for this the specification is not enabled. Therefore, the instant invention remains rejected as not being enabled for using an *O. gratissimum* extract for the treatment of a virus infected cell that can be found in an individual. The specification does not provide sufficient guidance for the inhibition of a HIV viral infection in a patient with an extract of *O. gratissimum*. There is not indication that high enough concentrations of the compound can be achieved in the patient to effect the viral replication *in vivo*. It is not a straightforward process to go from *in vitro* data to an *in vivo* treatment. Thus, the lack of working examples regarding treatment of HIV infection in a patient or animal model, the lack of guidance in the specification, and the unpredictability regarding extrapolating *in vitro* data to an *in vivo* treatment method greatly reduces the probability that one of skill in the art would successfully obtain the claimed invention without undue experimentation.

(4) Predictability of *in vitro* data to *in vivo* test results. Appellants argument is that "it is well established under U.S. patent law and practice that *in vitro* results with respect to the particular pharmacological activity can be predictive of *in vivo* test results, if there is a reasonable correlation there between."

In response, in this instance there is no established correlation in viral therapies between *in vitro* test results and *in vivo* function. Thus, in the field of HIV, or viral therapy in general,

there is no predictability to *in vivo* function when using *in vitro* tests only to establish that a drug has an effect on the virus.

Appellants cite Hoggard et al., Havilir et al. and King et al. in a footnote in their appeal brief for the proposition that *in vitro* models can be predicative of the clinical situation when using combination therapy.

In response, this is the first time that the references of Hoggard et al., Havilir et al. and King et al. have been cited to the Office, the references have not been provided on a 1449 thus the contents of the references have not been fully considered. However, as far as the statement made that for combination therapy the *in vitro* results can be predictive of an *in vivo* effect. The combination therapies contemplated in the references indicate that each of the compounds was known to individually inhibit HIV in a patient before the testing of the effect of the combination in *in vitro* assays. Here the *in vitro* assay tested known drugs that have been shown individually to be effective against HIV *in vivo* in a patient. The testing in the cited references differs from the instant *in vitro* assay because the individual compounds already had a proven track record of being tolerated by a patient population. In the instant invention the plant extract has not been shown to be to be effective against HIV in an individual. It has not been established that the extract can be given to a patient in a sufficient amount to be effective and to be tolerated in the patient. Just because a composition can be given to a cell in a tissue culture plate at sufficient concentration to be effective at inhibiting the cytopathic effect of a virus in tissue culture does not indicate that the same composition can be given to a patient in an effective amount that will inhibit the cytopathic effect of the virus in the patient. The effective amount to inhibit the

cytopathic effect of a virus in a patient can be at a concentration that is either toxic or lethal to the patient.

Appellants cite Ayisi et al. in a footnote in their appeal brief for the proposition that AZT was tested in *in vitro* models along side the plant extract and that this testing provides support for the therapeutic potential of the plant extracts. Appellants attempt to use AZT a known compound that has been proven to be effective in a patient for the purpose of inhibiting HIV and to correlate the known *in vivo* effect of AZT with the unknown *in vivo* effect of the plant extract.

In response, this is the first time that the references of Ayisi et al. has been cited to the Office, the references has not been provided on a 1449 thus the contents of the references has not been fully considered. However, the comparison of AZT in an *in vitro* environment with the plant extract in the *in vitro* environment cannot provide the correlation to establish that the plant extracts would work in the same manner as AZT would work in the *in vivo* environment. AZT is a known compound that is known to work *in vivo* in a patient and that has been established to be effective at doses that are not toxic to a patient. The experimental results in the cited reference and the results show in the instant specification does not provide any insight into whether the plant extracts can be administered to a patient at high enough concentration to be effective and to not be toxic. Suramin was shown in a prior reference to be very promising in *in vitro* studies to block the infectability of HIV, however, *in vivo* experiments using suramin demonstrate no significant clinical or immunological improvement and in this case the net effect of suramin was in fact harmful.

(5) Enablement. Appellants' argument is that the Office has improperly relied to heavily on the unpredictability in the correlation of the *in vitro* assay with *in vivo* efficacy.

In response, the best examples of the unpredictability of the efficacy of the plant extract for the treatment of HIV comes from the use of the decoction (boiling leaves in water to make tea) *O. gratissimum* in the use of herbal medicine in Africa (see El-Said et al. cited in the 35 USC 102(b) rejection). Here Nigerian people used an infusion of the *O. gratissimum* for the purpose of treating fevers, fevers are a response by the body to combat bacterial or viral infections. The Nigerian patient may not have appreciated the nuance that a compound found in the plant actually has a cytophatic effect on a virus in a test tube. The purpose of drinking the infusion of *O. gratissimum* by a patient is to help the patient get well. Though the use of the infusion of the *O. gratissimum* (an aqueous extract) has been known and used in Africa for years the use of the herbal medicine does not appear to have an effect against HIV because Africa remains to be the center of the global HIV infection and the rates of infection in the population in Africa is higher than anywhere else in the world. Although the extract of *O. gratissimum* can be effective against other viral pathogens in a patient, from empirical observation there is no indication that the use of the infusion of this plant which is well known in African herbal medicine is effective against HIV. It may be that the effective ingredient of the extract cannot get to the site of HIV viral infection at a high enough concentration to be effective to treat HIV in a patient.

Issue 2 – 35 USC §102(b)

Appellants argument is that "a claim is anticipated only if each and every element as set forth in the claim is found either, expressly or inherently in a single prior art reference." *Verdegaal Bros. V. Union. Oil of California*, 814 F2d 628, 2 USPQ 2d 1051, (Fed Cir. 1987). Appellants have repeatedly made the argument that the El-Said et al. reference has only tested the effect of the extract *Ocimum gratissimum* on bacterial growth. Appellants argument is that because the El-Said et al. reference has not specifically tested the effect of *O. gratissimum* extract on virally infected cells therefore the composition (extract) is not capable of having the effect that the composition inhibits the cytopathic effect of the virus in a cell. Appellants' argument is that because the reference does not disclose the testing of the extract against the cytopathic effect of a virus then the reference cannot disclose each and every element.

In response, Appellants are requiring that the claimed elements are literally present in the reference, this is not the law as set out in *Verdegaal Bros. V. Union. Oil of California*, 814 F2d 628, 2 USPQ 2d 1051, (Fed Cir. 1987). The elements may be inherently present in a reference; in this case the reference teaches "in Nigeria, a decoction (boiling leaves in water) of *O. gratissimum* is used in the treatment of fever." The plant is widely cultivated in Nigeria so that it may be used for medicinal purposes.

Here the claim recites using an old composition an extract of *O. gratissimum* for the purpose of inhibiting the cytopathic effect of the virus. "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art..... However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the

discoverer." The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art." *Atlas Powder Co. V. IRECO,* 51 USPQ2d 1943 (Fed. Cir. 1999)

The mere recitation of newly-discovered function or property, inherently possessed by things in the prior art, does not cause the claim drawn to those things to distinguish over the prior art (See *In re Best, Bolton, and Shaw* 195 USPQ 430 (CCPA 1977), *In re Schreiber* 44 USPQ2d 1429). *In re Best* is directed to a particular set of circumstances where examiners in the USPTO cannot readily determine whether a difference exists between the subject matter of a given claim and a particular prior art document. Typically these circumstances arise in the context of a claim directed to a compound or composition where the claim describes a property or a function of the compound or composition which the prior art reference does not address, as in the present situation. MPEP 2131.01 provides that normally, only one reference should be used in making a rejection under 35 USC §102. However, a 35 USC §102 rejection over multiple references has been held to be proper when the extra references are cited to: (a) prove the primary reference contains an "enabled disclosure;" (b) explain the meaning of a term used in the primary reference; or (c) show that a characteristic not disclosed in the reference is inherent. Extra references or evidence can be used to show an inherent characteristic of the thing taught by the primary reference. "To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d

1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation.

Appellants have provided a description of the differences between bacteria and viruses. The Office does not dispute that there are differences between bacteria and viruses. Appellants have made a point that in modern medicine practitioners often first investigate whether a virus causes the symptoms or whether the symptoms are caused by a bacterium before rendering treatment, so that the treatment will be pathogen specific. Appellants' state, "that a blood test showing a decreased white blood cell count is indicative of a viral infection."

In response, the claims do not require specific method steps that distinguish between a viral and bacterial infection before rendering treatment. The argument that a blood test could distinguish between a bacterial or a viral infection is not relevant because the claims do not require such a specific step. Furthermore, it is not unusual encounter both bacterial and viral infections at the same time in a patient. Often after a patient becomes infected with a virus infection they develop an opportunistic bacterial infection. In this instance, the claims only require the single step of contacting a virally infected cell with the extract. The patient getting better shows the limitation of "in an amount effective enough to inhibit the cytopathic effect of the virus in the cell." Thus a patient having fever caused by a virus who drinks a decoction made from *O. gratissimum* followed by recovering would be practicing the instantly claimed invention.

Appellants additionally argue that the cited reference must provide an enabling disclosure, citing *In re Hoeksema*, 399 F2d 269, 158 USPQ 596 (CCPA 1968).

In response, Appellants in their specification have made aqueous extracts by boiling the leaves, seeds, fruits, stems, barks or roots in distilled water for 10 min (see specification page 6, lines 18-21). The instant invention reads on treatment of a viral infection *in vivo* using an extract of *Ocimum gratissimum*. El-Said et al. discloses that an extract (a decoction which is boiling leaves in water like tea) of *O. gratissimum* has been used in Nigerian herbal medicine for the treatment of fevers (see abstract). Fever is a symptom that is associated with viral or bacterial infections, this is evidenced by the Merck Manual. Therefore, the treatment of viral infection using an extract of *O. gratissimum* is anticipated by El-Said et al.

Appellants argue that a claim is anticipated only if each and every element is expressly or inherently described in the art reference (MPEP 2131) and a reference contains an enabling disclosure if the public was in possession of the claimed invention before the date of the invention (MPEP 2121.01).

In response, the prior art discloses the decoction (boiling leaves in water like tea) of *O. gratissimum* for the treatment of fever and diaphoretic and also as a stomachic laxative. The prior art and Appellants disclosure use the same method of extracting the ingredient from the plant by boiling the plant in water.

Appellants' arguments are that the reference only discloses the preparation and testing of (a) an aqueous extract of the whole plant (b) the essential oil and (c) an aqueous solution of the

essential oil for the ability to inhibit bacterial growth. The reference does not disclose anti-viral testing and/or a method of use *O. gratissimum* for inhibiting the cytopathic effects of a virus infected cell.

In response, where a method of the prior art is performed on either the same population or a subset of the same population as the claimed method using the same material and methodology, the prior art method inherently would achieve whatever desired outcome was discovered and claimed by applicant. Here Nigerian people used an infusion of the *O. gratissimum* for the purpose of treating fevers, fevers are a response by the body to combat bacterial or viral infections. The Nigerian patient may not have appreciated the nuance that a compound found in the plant actually has a cytopathic effect on a virus in a test tube. The purpose of drinking the infusion of *O. gratissimum* by a patient is to help the patient get well. Applicants are asking that the Office grant them a patent where the Nigerian patient, who happens to be infected with a virus, would be infringing the instant claim by drinking tea made from *O. gratissimum*. The prior art discloses a method of administering an extract of *O. gratissimum* to a patient and the compounds responsible for inhibiting a virus would inherently be present in the extract. *In re Cruciferous Sprout Litigation,* 64 USPQ2d 1202 (CA FC 2002).

Appellants cite *In re Marshal*, 578 F2d 301, 198 USPQ 344 (CCPA 1978) for the proposition that the PDR reference could not function as prior art because there was nothing in the PDR to suggest using the composition for the purpose of weight loss.

In response, the facts of in *Marshal* can be distinguished from the instant facts. In *Marshal* the PDR was silent regarding weight loss and thus the PDR could not establish that the

drug would be effective for weight loss. In the reference of El-Said et al. the Nigerian people used an extract of *O. gratissimum* for the purpose of treating fevers. The reference is not silent for what purpose the extract was used, after reading the reference the ordinary artisan would know to use the extract to treat fever. Because fever is a symptom of a viral infection the treatment of fever by ingesting the extract plant comprises a method of contacting a virally infected cell with the extract. That fevers can be caused by other infections does not take away form the knowledge of the folk healer to use the extract for the purpose of treating a fever. Thus the use of the extract to treat a viral infection is not the result of an "unrecognized accident." Here the Nigerian folk healer used the aqueous infusion (i.e. tea) of the plant *O. gratissimum* to help his patient feel better.

The instant invention reads on treatment of a viral infection *in vivo* using an extract of *O. gratissimum*. El-Said et al. disclose that use of an extract of *O. gratissimum* has been used in Nigerian herbal medicine for the treatment of fevers (see abstract). Fever is a symptom that is associated with viral or bacterial infections. Thus, the treatment of viral infection using an extract of *O. gratissimum* is anticipated by El-Said et al. and should be maintained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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